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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,858	08/29/2001	Jorge Plutzky	81994/282421	5046

7590

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EXAMINER

CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT

PAPER NUMBER

1615

DATE MAILED: 03/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/940,858

Applicant(s)

PLUTZKY ET AL.

Examiner

Lakshmi S Channavajjala

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 12-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

Receipt of request for extension of time, response to election requirement, amendment A and change of address, all dated 12-30-02 is acknowledged.

#### ***Election/Restrictions***

Applicant's election without traverse of Group III (claims 12-16) in Paper No. 8 is acknowledged.

Non-elected claims 1-11 and 17-23 have been canceled.

Claims 12-16 are pending prosecution. Instant claims are directed to a method of treating a patient for atherosclerosis comprising administering a therapeutically effective amount of a compound selected from the group consisting of oxidized all-trans retinoic acid, oxidized 9-cis retinoic acid and reduced 4-oxo-retinoic acid.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaish et al (J. Clin. Invest. 1995; hereafter referred to as Shaish) alone OR Shaish in view of Samokyszyn et al (J. Biol. Chem. 1987; hereafter referred to JBC).

Shaish teaches that oxidatively damaged low-density lipoproteins play an important role in atherogenesis and showed that all-trans isomers of beta-carotene inhibited the formation of atherogenic lesions. Further, Shaish teaches that the metabolites of all-trans-forms of beta-carotene inhibit atherosclerosis. Shaish does not teach the oxidized all-trans or oxidized 9-cis-retinoic acid as claimed in the instant claims. Shaish does not teach the claimed dosages of the compounds.

JBC studied the hydroperoxide-dependent oxidation of 13-cisretinoic acid in microsomes by prostaglandin synthase and teaches the major oxygenated metabolites such as 4-hydroxy, 5,6-epoxy, 5,8-oxo-13-cis –retinoic acid etc. Further, JBC teaches isomerization of all-trans –retinoic acid to 13-cis configuration has been observed during oxidative metabolism to the 4-oxo metabolite (page 14129). JBC further teaches that oxidation products of cis-retinoic acid and all trans-retinoic acid are effective in scavenging free radicals, (in the context of lipid peroxidation as well as tumor promotion) and further suggest that epoxide retinoic acids may actually represent a pharmacologically active form of retinoic acid and even further, hydroperoxide-dependent cooxidation of 13-cis-retinoic acid by prostaglandin synthase represents a metabolic activation. While JBC does not teach the specific oxidized retinoic acid compounds claimed, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention

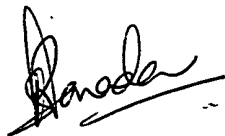
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to use oxidized forms of cis- or all-trans isomers of retinoic acid for the treatment of atherosclerosis because JBC teaches that epoxy products (a result of oxidation) of cis-retinoic or trans retinoic acids represent the metabolically active forms of retinoic acid. Accordingly, one of an ordinary skill in the art would have used oxidized retinoic (cis as well as trans) in the teachings of Shaish, with an expectation to inhibit lipid peroxidation and in turn inhibit atherosclerosis. Further, it would have been within the scope of a skilled artisan to use appropriate amounts of oxidized retinoic acids with an expectation to achieve the art recognized effect.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Lakshmi S Channavajjala  
Examiner  
Art Unit 1615  
March 21, 2003